For mild or moderate typhoid caused by multidrug-resistant strains, 500 mg once daily may be given for 7 days.

For details of doses in infants and children, see below.

Azithromycin dihydrate may also be given initially by intravenous infusion to adults in doses equivalent to 500 mg of azithromycin as a single daily dose in the treatment of community-acquired pneumonia and pelvic inflammatory disease; treatment should be changed to the oral route after at least 2 days in pneumonia and after 1 or 2 days in pelvic inflammatory disease. It may be given either in a solution containing 1 mg/mL over 3 hours or in a solution containing 2 mg/mL over 1 hour.

In the USA, azithromycin is available as 1% eye drops for the topical treatment of conjunctivitis caused by susceptible strains of bacteria.

◊ Reviews.

1. Peters DH, *et al.* Azithromycin: a review of its antimicrobial activity, pharmacokinetic properties and clinical efficacy. *Drugs* 1992; **44:** 750–99.
2. Langtry HD, Balfour JA. Azithromycin: a review of its use in paediatric infectious disease. *Drugs* 1998; **56:** 273–97.
3. Alvarez-Elcoro S, Enzler MJ. The macrolides: erythromycin, clarithromycin, and azithromycin. *Mayo Clin Proc* 1999; **74:** 613–34.
4. Garey KW, Amsden GW. Intravenous azithromycin. *Ann Pharmacother* 1999; **33:** 218–28.
5. Ioannidis JPA, *et al.* Meta-analysis of randomized controlled trials on the comparative efficacy and safety of azithromycin against other antibiotics for upper respiratory tract infections. *J Antimicrob Chemother* 2001; **48:** 677–89.
6. Contopoulos-Ioannidis DG, *et al.* Meta-analysis of randomized controlled trials on the comparative efficacy and safety of azithromycin against other antibiotics for lower respiratory tract infections. *J Antimicrob Chemother* 2001; **48:** 691–703.
7. Zuckerman JM. Macrolides and ketolides: azithromycin, clarithromycin, telithromycin. *Infect Dis Clin North Am* 2004; **18:** 621–49.
8. Law C, Amsden GW. Single-dose azithromycin for respiratory tract infections. *Ann Pharmacother* 2004; **38:** 433–9.
9. Blumer JL. Evolution of a new drug formulation: the rationale for high-dose, short-course therapy with azithromycin. *Int J Antimicrob Agents* 2005; **26** (suppl 3): S143–S147.
10. Swainston Harrison T, Keam SJ. Azithromycin extended release: a review of its use in the treatment of acute bacterial sinusitis and community-acquired pneumonia in the US. *Drugs* 2007; **67:** 773–92.
11. Panpanich R, *et al.* Azithromycin for acute lower respiratory tract infections. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 18/06/08).

Administration in children. Azithromycin is licensed for use in infants and children and the usual oral dose in those over 6 months of age is 10 mg/kg once daily for 3 days, or an initial dose of 10 mg/kg may be followed by 5 mg/kg daily for a further 4 days; those who weigh over 45 kg may be given the usual adult dose (see above). A single dose of 30 mg/kg may also be given for acute otitis media. For pharyngitis or tonsillitis in children aged over 2 years, 12 mg/kg once daily for 5 days may be given.

US official guidelines suggest that for prophylaxis of disseminated *Mycobacterium avium* complex infections, azithromycin 20 mg/kg (to a maximum of 1.2 g) once weekly or 5 mg/kg (to a maximum of 250 mg) once daily may be given.[1] For treatment, 10 to 12 mg/kg (to a maximum of 500 mg) once daily should be given with other antimycobacterials.[2]

In the UK, the *BNFC* suggests that azithromycin may be used in penicillin allergic children for the prevention of secondary cases of group A streptococcal infection; those 6 months and older may be given an oral dose of 12 mg/kg (to a maximum of 500 mg) once daily for 5 days.

The *BNFC* also suggests giving azithromycin 10 mg/kg once daily for 7 days in the treatment of mild to moderate typhoid caused by multidrug-resistant strains in those aged 6 months and over.

1. CDC. Guidelines for preventing opportunistic infections among HIV-infected persons—2002: recommendations of the US Public Health Service and the Infectious Diseases Society of America. *MMWR* 2002; **51** (RR-8): 1–52. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5108.pdf (accessed 01/05/07)
2. CDC. Treating opportunistic infections among HIV-exposed and infected children: recommendations from CDC, the National Institutes of Health, and the Infectious Diseases Society of America. *MMWR* 2004; **53** (RR-14): 1–63. Also available at: http://www.cdc.gov/mmwr/PDF/RR/RR5314.pdf (accessed 01/05/07)

Babesiosis. In a prospective, randomised study[1] involving 58 patients with babesiosis (p.823), azithromycin with atovaquone was found to be as effective as, and associated with fewer adverse effects than, standard therapy with quinine and clindamycin. Azithromycin 600 mg once daily, or 500 to 1000 mg on day 1 followed by 250 mg once daily thereafter, with atovaquone 750 mg twice daily, both orally for 7 to 10 days, has been recommended by some experts[2,3] in the USA for the treatment of *Babesia microti* infections. Immunocompromised patients may be given higher doses of azithromycin (600 to 1000 mg daily). Children may be given azithromycin 12 mg/kg once daily, or 10 mg/kg on day 1 followed by 5 mg/kg once daily thereafter, with atovaquone 20 mg/kg twice daily, both orally for 7 to 10 days. Azithromycin with quinine was reported to be effective in 2 patients who had not responded to quinine plus clindamycin.[4,5]

1. Krause PJ, *et al.* Atovaquone and azithromycin for the treatment of babesiosis. *N Engl J Med* 2000; **343:** 1454–8.
2. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
3. Wormser GP, *et al.* The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006; **43:** 1089–1134. Also available at: http://www.journals.uchicago.edu/doi/pdf/10.1086/508667 (accessed 12/08/08)
4. Shaio MF, Yang KD. Response of babesiosis to a combined regimen of quinine and azithromycin. *Trans R Soc Trop Med Hyg* 1997; **91:** 214–15.
5. Shih C-M, Wang C-C. Ability of azithromycin in combination with quinine for the elimination of babesial infection in humans. *Am J Trop Med Hyg* 1998; **59:** 509–12.

Cholera. Azithromycin has been tried[1-3] in the treatment of cholera (p.172). A single dose of 10 or 20 mg/kg was found to be effective in children[1,2] and 1 g in adults.[3]

1. Khan WA, *et al.* Comparison of single-dose azithromycin and 12-dose, 3-day erythromycin for childhood cholera: a randomised, double-blind trial. *Lancet* 2002; **360:** 1722–7.
2. Bhattacharya MK, *et al.* Azithromycin in the treatment of cholera in children. *Acta Paediatr* 2003; **92:** 676–8.
3. Saha D, *et al.* Single-dose azithromycin for the treatment of cholera in adults. *N Engl J Med* 2006; **354:** 2452–62.

Hyperplasia. For reference to the use of azithromycin to control ciclosporin-induced gingival hyperplasia, see p.1824.

Ischaemic heart disease. Macrolide antibacterials, including azithromycin,[1-4] clarithromycin,[5-9] and roxithromycin,[10-14] have been investigated in the prevention of ischaemic heart disease, based on a suggested link between atherosclerosis and infection with *Chlamydophila pneumoniae* (*Chlamydia pneumoniae*) (see p.166). Although preliminary results from some pilot studies were promising, longer-term studies in large numbers of patients were disappointing and none of the three macrolides decreased ischaemic events or provided clinical benefit; indeed, in one study[9] an unexpected increase in cardiovascular mortality was seen in those taking clarithromycin.

1. Anderson JL, *et al.* Randomized secondary prevention trial of azithromycin in patients with coronary artery disease and serological evidence for Chlamydia pneumoniae infection: the Azithromycin in Coronary Artery Disease: Elimination of Myocardial Infection with Chlamydia (ACADEMIC) study. *Circulation* 1999; **99:** 1540–7.
2. Cercek B, *et al.* Effect of short-term treatment with azithromycin on recurrent ischaemic events in patients with acute coronary syndrome in the Azithromycin in Acute Coronary Syndrome (AZACS) trial: a randomised controlled trial. *Lancet* 2003; **361:** 809–13.
3. O'Connor CM, *et al.* Azithromycin for the secondary prevention of coronary heart disease events: the WIZARD study: a randomized controlled trial. *JAMA* 2003; **290:** 1459–66.
4. Grayston JT, *et al.* Azithromycin for the secondary prevention of coronary events. *N Engl J Med* 2005; **352:** 1637–45.
5. Sinisalo J, *et al.* Effect of 3 months of antimicrobial treatment with clarithromycin in acute non-Q-wave coronary syndrome. *Circulation* 2002; **105:** 1555–60.
6. Berg HF, *et al.* Effect of clarithromycin on inflammatory markers in patients with atherosclerosis. *Clin Diagn Lab Immunol* 2003; **10:** 525–8.
7. Berg HF, *et al.* Treatment with clarithromycin prior to coronary artery bypass graft surgery does not prevent subsequent cardiac events. *Clin Infect Dis* 2005; **40:** 358–65.
8. Berg HF, *et al.* Effect of clarithromycin treatment on Chlamydia pneumoniae in vascular tissue of patients with coronary artery disease: a randomized, double-blind, placebo-controlled trial. *J Clin Microbiol* 2005; **43:** 1325–9.
9. Jespersen CM, *et al.* Randomised placebo controlled multicentre trial to assess short term clarithromycin for patients with stable coronary heart disease: CLARICOR trial. *BMJ* 2006; **332:** 22–7. Correction. *ibid.*; 151.
10. Gurfinkel E, *et al.* Treatment with the antibiotic roxithromycin in patients with acute non-Q-wave coronary syndromes: the final report of the ROXIS Study. *Eur Heart J* 1999; **20:** 121–7.
11. Wiesli P, *et al.* Roxithromycin treatment prevents progression of peripheral arterial occlusive disease in Chlamydia pneumoniae seropositive men: a randomized, double-blind, placebo-controlled trial. *Circulation* 2002; **105:** 2646–52.
12. Zahn R, *et al.* Antibiotic therapy after acute myocardial infarction: a prospective randomized study. *Circulation* 2003; **107:** 1253–9.
13. Sander D, *et al.* Progression of early carotid atherosclerosis is only temporarily reduced after antibiotic treatment of Chlamydia pneumoniae seropositivity. *Circulation* 2004; **109:** 1010–15.
14. Kaehler J, *et al.* A randomized trial in patients undergoing percutaneous coronary angioplasty: roxithromycin does not reduce clinical restenosis but angioplasty increases antibody concentrations against Chlamydia pneumoniae. *Am Heart J* 2005; **150:** 987–93.

Malaria. Azithromycin has been studied[1-7] in the management of malaria. Studies[1,4] have shown that an initial loading dose of 750 mg of azithromycin on the first day followed by 250 mg daily thereafter for 20 weeks was effective in the prophylaxis of *Plasmodium vivax* malaria; the drug was well tolerated and the most frequently reported adverse effects were heartburn, paraesthesia, and itching.[3] In the treatment of *P. vivax* malaria, a study[5] found that azithromycin 1 g daily for 3 days resulted in an 88% clinical response rate by day 7, but with a slower onset of action, when compared with chloroquine 600 mg daily for 2 days then 300 mg on day 3 which resulted in a rate of 99%.

Azithromycin in a dose of 0.5 g once daily up to 1.5 g daily in divided doses together with other antimalarials, such as artesunate 200 mg daily[2,7] or quinine 10 mg/kg 3 times daily,[6,7] given for 3 days was found to be effective in the treatment of uncomplicated multidrug-resistant *P. falciparum* malaria.

However, further studies are warranted, especially in children and pregnant women.

1. Taylor WR, *et al.* Malaria prophylaxis using azithromycin: a double-blind, placebo-controlled trial in Irian Jaya, Indonesia. *Clin Infect Dis* 1999; **28:** 74–81.
2. Krudsood S, *et al.* A randomized clinical trial of combinations of artesunate and azithromycin for treatment of uncomplicated Plasmodium falciparum malaria in Thailand. *Southeast Asian J Trop Med Public Health* 2000; **31:** 801–7.
3. Taylor WR, *et al.* Tolerability of azithromycin as malaria prophylaxis in adults in Northeast Papua, Indonesia. *Antimicrob Agents Chemother* 2003; **47:** 2199–2203.
4. Heppner DG, *et al.* Randomized, controlled, double-blind trial of daily oral azithromycin in adults for the prophylaxis of Plasmodium vivax malaria in Western Thailand. *Am J Trop Med Hyg* 2005; **73:** 842–9.
5. Dunne MW, *et al.* A double-blind, randomized study of azithromycin compared to chloroquine for the treatment of Plasmodium vivax malaria in India. *Am J Trop Med Hyg* 2005; **73:** 1108–11.
6. Miller RS, *et al.* Effective treatment of uncomplicated Plasmodium falciparum malaria with azithromycin-quinine combinations: a randomized, dose-ranging study. *Am J Trop Med Hyg* 2006; **74:** 401–6.
7. Noedl H, *et al.* Azithromycin combination therapy with artesunate or quinine for the treatment of uncomplicated Plasmodium falciparum malaria in adults: a randomized, phase 2 clinical trial in Thailand. *Clin Infect Dis* 2006; **43:** 1264–71.

Respiratory disorders. For reference to the use of azithromycin in the management of respiratory disorders, see under Erythromycin, p.273.

Preparations

USP 31: Azithromycin Capsules.

Proprietary Preparations (details are given in Part 3)

Arg.: Arzomicin; Azitral; Azitrogal; Azitrolan; Azitrona; Azitrox; Clearsing; Cronopen; Doyle; Fabramicina; Finatres†; Macromax; Misultina; Naxocina; Neblic; Nifostin; Novozitron; Orobiotic; Sitrox; Sumir†; Talcilina; Tanezox; Triamid; Tritab; Vectocilina; Zitromax; ***Austral.:*** Zithromax; ***Austria:*** Zithromax; ***Belg.:*** Zitromax; ***Braz.:*** Astro; Atromicin; Azatill; Azi; Azidromic†; Azimed; Azimix; Azitrax†; Azitrin; Azitrogran; Azitrolab; Azitromicil; Azitromin†; Azitron; Azitronax†; Azitroxil; Biozitrom†; Clindal; Ems-Max; Mac Azi; Mazitrom; Novatrex; Selimax; Selimax Pulso; Siftromin†; Triazi†; Tromix; Trozyman; Zimicina†; Zitril; Zitromax; Zitromil; Zitroneo; ***Canad.:*** Z-Pak; Zithromax; ***Chile:*** Abacten; Aspiral†; Atizor; Azitrom; Ricilina; Trex; Zithromax; ***Cz.:*** Azibiot; Azitrox; Sumamed; Zitrocin; ***Denm.:*** Zitromax; ***Fin.:*** Zithromax; ***Fr.:*** Azadose; Zithromax; ***Ger.:*** Ultreon; Zithromax; ***Gr.:*** Azibactron; Azifarm; Azirox; Azirutec; Azithral; Azithrin; Azitrolid; Azivirus; Azytan; Bezanin; Disithrom; Figothrom; Goldamycin; Gramokil; Novozithron; Zinfect; Zithro-Due; Zithromax; Zithropan; Zithrotel; Zithroxyn; Zitrax; ***Hong Kong:*** Zithromax; ***Hung.:*** Azi; Azicid; Sumamed; Zitrocin; ***India:*** Azee; Azibact; Azifast; Azithral; Aziwok; Zithrocin; Zycin; ***Indon.:*** Aztrin; Binozyt; Mezatrin; Zarom; Zibramax; Zicho; Zifin; Zistic; Zithromax; Zycin; ***Irl.:*** Azromax; Zithromax; ***Israel:*** Azenil; Zeto; Zithromax; ***Ital.:*** Azitrocin; Ribotrex; Trozocina; Zitromax; ***Malaysia:*** Zithromax; ***Mex.:*** Amsati; Azibiot; Aziphar; Azitrocin; Azitrohexal; Azo-Max; Koptin; Macrozit; Medatz; Sicalan; Texis; Tromicina; Truxa; Zertalin; Zithran; Zitroken; ***Neth.:*** Azacleus; Azitro; Merckazitro; Nucaza; Zithromax; ***Norw.:*** Azitromax; ***NZ:*** Zithromax; ***Philipp.:*** Zithromax; ZMax; ***Pol.:*** Azibiot; Azimycin; Azitrox; Macromax; Oranex; Sumamed; ***Port.:*** 3Z; Arzomicina†; Azimax; Aziton; Azitrix; Biozitra; Gigatrom; Lazitrom; Neofarmiz; Unizitro; Vascin; Zithromax; Zitrozina; ***Rus.:*** Azithrox (Азитрокс); Azithrus (Азитрус); Azitral (Азитрал); Aziwok (Азивок); Hemomycin (Хемомицин); Sumamed (Сумамед); Zetamax (Зетамакс); ZI-Factor (ЗИ-фактор); Zithrocin (Зитроцин); Zitrolid (Зитролид); ***S.Afr.:*** Zithrogen; Zithromax; ***Singapore:*** Zithromax; ***Spain:*** Altezym; Goxil; Pefloden; Toraseptol; Vinzam; Zentavion; Zitromax; ***Swed.:*** Azitromax; ***Switz.:*** Zithromax; ***Thai.:*** Binozyt; Zithromax; ***Turk.:*** Azacid; Azeltin; Azitro; Azomax; Azro; Tremac; Zitromax; Zitrotek; ***UAE:*** Azomycin; ***UK:*** Zithromax; ***USA:*** AzaSite; Zithromax; Zmax; ***Venez.:*** Amizin; Amovin; Aruzilina; Arzomidol; Atromizin; Azigram; Azimakrol; Azitrom; Azitromin; Binozyt; Saver; Zitromax; Zival.

Multi-ingredient: ***India:*** Orflaz Kit; Safkit; ***Mex.:*** Zithroflam.

Azlocillin *(BAN, USAN, rINN)*

Atslosilliini; Azlocilina; Azlocilline; Azlocillinum. 6-[*N*-(2-Oxoimidazolidin-1-ylcarbonyl)-D-phenylglycylamino]penicillanic acid.

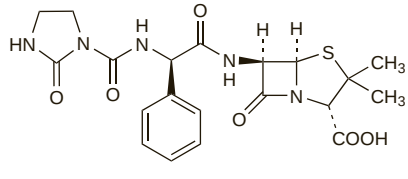
Азлоциллин

$C_{20}H_{23}N_5O_6S$ = 461.5.

CAS — 37091-66-0.

ATC — J01CA09.

ATC Vet — QJ01CA09.



Azlocillin Sodium *(BANM, rINNM)*

Azlocilina sódica; Azlocilline Sodique; Azlocillinum Natricum; Azlocylina sodowa; Bay-e-6905; Natrii Azlocillinum. Sodium (6*R*)-6-[D-2-(2-oxoimidazolidine-1-carboxamido)-2-phenylacetamido]penicillanate.

Натрий Азлоциллин

$C_{20}H_{22}N_5NaO_6S$ = 483.5.

CAS — 37091-65-9.

ATC — J01CA09.

ATC Vet — QJ01CA09.

Pharmacopoeias. In *Pol.*

Incompatibility. Azlocillin sodium has been reported to be incompatible with aminoglycosides, ciprofloxacin, metronidazole, and tetracyclines.

Adverse Effects and Precautions

As for Carbenicillin Sodium, p.216.

Prolongation of bleeding time has been less frequent and less severe with azlocillin than with carbenicillin.

Hypouricaemia. Reports of transient asymptomatic decreases in serum-uric acid concentrations during treatment with azlocillin.[1,2]

1. Faris HM, Potts DW. Azlocillin and serum uric acid. *Ann Intern Med* 1983; **98:** 414.
2. Ernst JA, Sy ER. Effect of azlocillin on uric acid levels in serum. *Antimicrob Agents Chemother* 1983; **24:** 609–10.

Sodium content. Each g of azlocillin sodium contains about 2.1 mmol of sodium. As azlocillin sodium has a lower sodium content than carbenicillin sodium, hypernatraemia and hypokalaemia are less likely to occur.

Interactions

As for Benzylpenicillin, p.214.

Antibacterials. For the effect of azlocillin on the clearance of *cefotaxime*, and a report of neurotoxicity, see p.228. For reference to azlocillin affecting the disposition of *ciprofloxacin*, see p.246.

Antimicrobial Action

Azlocillin has an antimicrobial action similar to that of piperacillin (p.315). Its activity *in vitro* against Enterobacteriaceae is generally less than that of mezlocillin or piperacillin, but it has comparable activity to piperacillin against *Pseudomonas aeruginosa*.

Pharmacokinetics

Azlocillin is not absorbed from the gastrointestinal tract to any significant extent. It has nonlinear dose-dependent pharmacokinetics. Doubling an intravenous dose results in more than double the plasma concentration. Between 20 and 46% of azlocillin in the circulation is bound to plasma proteins. The plasma half-life is usually about 1 hour, but is longer in neonates; in patients with renal impairment half-lives of 2 to 6 hours have been reported.

Azlocillin is widely distributed in body tissues and fluids. It crosses the placenta into the fetal circulation and small amounts are distributed into breast milk. There is little diffusion into the CSF except when the meninges are inflamed.

Azlocillin is metabolised to a limited extent. About 50 to 70% of a dose is excreted unchanged in the urine by glomerular filtration and tubular secretion within 24 hours of a dose, resulting in high urinary concentrations. Azlocillin is partly excreted in the bile where it is also found in high concentrations.

Plasma concentrations are enhanced if probenecid is given.

Azlocillin is removed by haemodialysis.

Uses and Administration

Azlocillin is a ureidopenicillin and, like piperacillin (p.316), is used mainly for the treatment of infections caused by *Pseudomonas aeruginosa*. It has been used particularly for septicaemia, and infections of the respiratory and urinary tracts, and also for peritonitis; for details of these infections, see under Choice of Antibacterial, p.162.

Azlocillin is commonly used with an aminoglycoside; however, they should be given separately as they have been shown to be incompatible (see Incompatibility, above).

Administration and dosage. Azlocillin is given intravenously as the sodium salt. Doses are expressed in terms of the equivalent amount of azlocillin; 1.05 g of azlocillin sodium is equivalent to about 1 g of azlocillin. A 10% solution in a suitable diluent is given by slow injection for doses of 2 g or less; higher doses should be infused over 20 to 30 minutes.

The usual adult dose is 5 g every 8 hours for life-threatening infections, or 2 g every 8 hours for less severe infections and urinary-tract infections.

The following doses may be used for children: premature infants, 50 mg/kg twice daily; neonates less than 7 days old, 100 mg/kg twice daily; infants between 7 days and 1 year, 100 mg/kg three times daily; children up to 14 years, 75 mg/kg three times daily.

Dosage of azlocillin may need to be adjusted in patients with hepatic or renal impairment (see below).

Administration in hepatic or renal impairment. The interval between doses of azlocillin may need to be increased to every 12 hours in moderate to severe renal impairment (creatinine clearance less than 30 mL/minute); additional dosage reductions may be needed in patients with both severe renal and hepatic impairment.

Aztreonam *(BAN, USAN, rINN)*

Atstreonaami; Azthreonam; Aztréonam; Aztreonamum; SQ-26776. (*Z*)-2-{2-Aminothiazol-4-yl-[(2*S*,3*S*)-2-methyl-4-oxo-1-sulphoazetidin-3-ylcarbamoyl]methyleneamino-oxy}-2-methylpropionic acid.

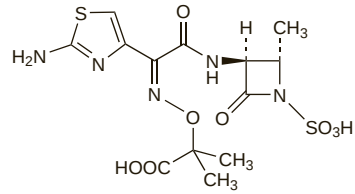
Азтреонам

$C_{13}H_{17}N_5O_8S_2$ = 435.4.

CAS — 78110-38-0.

ATC — J01DF01.

ATC Vet — QJ01DF01.



Pharmacopoeias. In *Jpn* and *US*, which allows the anhydrous or hydrated forms.

USP 31 (Aztreonam). A white, odourless crystalline powder. Very slightly soluble in dehydrated alcohol; practically insoluble in chloroform, in ethyl acetate, and in toluene; soluble in dimethylformamide and in dimethyl sulfoxide; slightly soluble in methyl alcohol. Store in airtight containers.

Incompatibility and stability. Aztreonam has been reported to be incompatible with cefradine, metronidazole, nafcillin, and vancomycin.

References.

1. Bell RG, *et al.* Stability of intravenous admixtures of aztreonam and cefoxitin, gentamicin, metronidazole, or tobramycin. *Am J Hosp Pharm* 1986; **43:** 1444–53.
2. Riley CM, Lipford LC. Interaction of aztreonam with nafcillin in intravenous admixtures. *Am J Hosp Pharm* 1986; **43:** 2221–4.
3. Belliveau PP, *et al.* Stability of aztreonam and ampicillin sodium-sulbactam sodium in 0.9% sodium chloride injection. *Am J Hosp Pharm* 1994; **51:** 901–4.
4. Trissel LA, Martinez JF. Compatibility of aztreonam with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1995; **52:** 1086–90.
5. Trissel LA, *et al.* Compatibility and stability of aztreonam and vancomycin hydrochloride. *Am J Health-Syst Pharm* 1995; **52:** 2560–4.

Adverse Effects

The adverse effects of aztreonam are similar to those of other beta lactams (see Benzylpenicillin, p.213, and Cefalotin, p.219). Hypersensitivity reactions, including skin rashes, urticaria, angioedema, exfoliative dermatitis, eosinophilia, bronchospasm, and rarely anaphylaxis and toxic epidermal necrolysis, may occur in patients receiving aztreonam, although it has been reported to be only weakly immunogenic. Gastrointestinal effects include diarrhoea, nausea, vomiting, mouth ulcer, and an abnormal taste.

Phlebitis or thrombophlebitis has been reported after the intravenous use of aztreonam, and pain or swelling after intramuscular injection.

Use of aztreonam may result in the overgrowth of non-susceptible organisms, including Gram-positive cocci. Pseudomembranous colitis or gastrointestinal bleeding may develop.

Other adverse effects that have been reported with aztreonam include jaundice and hepatitis, increases in liver enzymes, and prolongation of prothrombin and partial thromboplastin times.

Effects on the skin. References.

1. McDonald BJ, *et al.* Toxic epidermal necrolysis possibly linked to aztreonam in bone marrow transplant patients. *Ann Pharmacother* 1992; **26:** 34–5.

Precautions

Aztreonam should not be given to patients who are hypersensitive to it and should be used with caution in those known to be hypersensitive to other beta lactams, although the incidence of cross-sensitivity appears to be low (but see below).

Aztreonam should be used with caution in patients with renal or hepatic impairment.

Breast feeding. In a study in 12 healthy women given aztreonam, peak concentrations in breast milk were found to be less than 1% of those in serum and this was considered suggestive of a low risk of adverse effects in breast-fed infants.[1] The American Academy of Pediatrics states that no adverse effects have been seen in breast-fed infants whose mothers received aztreonam and considers it to be usually compatible with breast feeding,[2] although UK licensed product information recommends that mothers should refrain from breast feeding while receiving aztreonam.

1. Fleiss PM, *et al.* Aztreonam in human serum and breast milk. *Br J Clin Pharmacol* 1985; **19:** 509–11.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Hypersensitivity. Aztreonam is said to show little cross-reactivity with other beta lactams,[1,2] but there have been isolated reports of immediate hypersensitivity to aztreonam in patients with a history of hypersensitivity to penicillin.[3,4]

1. Saxon A, *et al.* Lack of cross-reactivity between aztreonam, a monobactam antibiotic, and penicillin in penicillin-allergic subjects. *J Infect Dis* 1984; **149:** 16–22.
2. Adkinson NF. Immunogenicity and cross-allergenicity of aztreonam. *Am J Med* 1990; **88** (suppl 3C): 12S–15S.
3. Alvarez JS, *et al.* Immediate hypersensitivity to aztreonam. *Lancet* 1990; **335:** 1094.
4. Hantson P, *et al.* Immediate hypersensitivity to aztreonam and imipenem. *BMJ* 1991; **302:** 294–5.

Interactions

Caution is recommended in patients receiving aztreonam and oral anticoagulants because of the possibility of increased prothrombin time.

Antimicrobial Action

Aztreonam is bactericidal and acts similarly to the penicillins by inhibiting synthesis of the bacterial cell wall; it has a high affinity for the penicillin-binding protein 3 (PBP-3) of Gram-negative bacteria. The activity of aztreonam is restricted to Gram-negative aerobic organisms, including beta-lactamase-producing strains, with poor or no activity against Gram-positive aerobes or anaerobic organisms. It is active against most Enterobacteriaceae including *Escherichia coli*, *Klebsiella*, *Proteus*, *Providencia*, *Salmonella*, *Serratia*, *Shigella*, and *Yersinia* spp. Some strains of *Enterobacter* and *Citrobacter* spp. are resistant. Aztreonam has some activity against *Pseudomonas aeruginosa*, although most strains of other *Pseudomonas* spp. are insensitive. Aztreonam has good activity against *Haemophilus influenzae* and *Neisseria* spp.

Synergy has been reported *in vitro* between aztreonam and aminoglycosides against *Ps. aeruginosa* and some *Enterobacteriaceae*.

Aztreonam is stable to hydrolysis by many beta-lactamases and appears to be a poor inducer of beta-lactamase production. Acquired resistance has occasionally been reported.

Pharmacokinetics

Aztreonam is poorly absorbed from the gastrointestinal tract and is therefore given parenterally. Absorption after intramuscular injection is good; peak plasma concentrations of about 46 micrograms/mL have been achieved within 1 hour of a 1-g dose. Aztreonam has a plasma half-life of about 1.7 hours. The half-life may be prolonged in neonates, in the elderly, in patients with renal impairment, and to some extent in those with hepatic impairment. Aztreonam is about 56% bound to plasma proteins. It is widely distributed in body tissues and fluids, including bile. Diffusion into the CSF is poor unless the meninges are inflamed. It crosses the placenta and enters the fetal circulation; small amounts are distributed into breast milk.

Aztreonam is not extensively metabolised. The principal metabolite, SQ-26992, is inactive and is formed by opening of the beta-lactam ring; it has a much longer half-life than the parent compound. Aztreonam is excreted mainly in the urine, by renal tubular secretion